UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte GERRIT D. MEULEMAN and PIETER ZANBERG

Appeal 2006-2868
Application 09/380,695
Technology Center 1600

ON BRIEF

Before GRIMES, LINCK, and LEBOVITZ, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of inhibiting atherosclerosis. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). Because we conclude that one of the references cited by the Examiner anticipates the pending claims, we vacate the appealed rejection and enter a new ground of rejection.

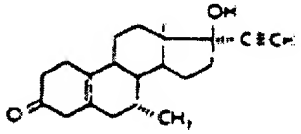
BACKGROUND

The Specification discloses that "atherosclerosis starts with the accumulation of cholesterol in lipoproteins in the vessel wall." (Specification 1.) "Coronary heart disease (CHD) is a consequence of

atherosclerotic processes in the artery vessel wall. . . . [I]ncidence of CHD in women in the reproductive stage of life is much lower than in men of similar age but . . . the risks sharply increase following the menopause." (*Id.*)

The Specification discloses that in peri- and post-menopausal women receiving estrogen replacement therapy, "exogenous estrogen is reported to have a plasma cholesterol- and a LDL (low density lipoproteins)-cholesterol lowering effect and/or a plasma HDL (high density lipoproteins)-cholesterol increasing effect. These estrogen effects may be suggestive of a protective overall effect on the formation of atherosclerotic lesions." (*Id.* at 2.)

The synthetic steroid tibolone (7α-methyl-17α-ethynyl-17β-hydroxy-estra-5(10)-en-3-one) has proven effective in estrogen replacement therapy. (*Id.*) Tibolone has the following chemical structure (see Haenggi,[1] Figure 1):



Early studies suggested that tibolone did not significantly affect patients' lipid profiles. (*Id.* at 2-3.) Later studies "emphasize the negative effect of tibolone on HDL levels (a decrease, which is associated with an increased CHD risk), but describe a ben[e]ficial decreasing effect found on lipoprotein(a) (Lp(a)) levels, which according to the authors may help to restore the balance of (cardiovascular) risks associated with tibolone therapy." (*Id.* at 3.)

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[1] Haenggi et al., "Postmenopausal Hormone Replacement Therapy with Tibolone Decreases Serum Lipoprotein(a)," *Eur. J. Clin. Chem. Clin. Biochem.*, Vol. 51, pp. 645-650 (1993).

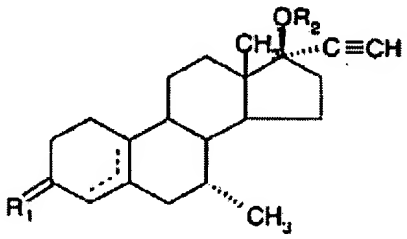
The Specification states that "[s]urprisingly, it has now been found that tibolone, prodrug forms thereof and certain metabolites thereof have strong anti-atherosclerotic properties." (*Id.*) These compounds are said to "have a strong intrinsic atheroprotective potential and are therefore not only useful drugs in hormone replacement therapy of peri- and post- menopausal women, but they are also suitable for therapeutic use in the treatment of atherosclerosis in mammals, both male and female, of all ages." (*Id.* at 6.)

DISCUSSION

1. CLAIMS

Claims 1-4 and 6 are pending and on appeal. Claim 1 reads as follows:

> 1. A method of inhibiting the atherosclerotic process, comprising administering to a mammal suffering from atherosclerosis an effective amount of a 7α-methyl-17α-ethynyl-estrane derivative having the general formula 1



Formula 1

wherein

R_1 = H(OR_3) or O;
R_2 = H or (C_{1-18})Acyl;
R_3 = H or (C_{1-18})Acyl;
and the dotted line represents a double bond in the 4, 5- or the 5, 10-position.

Thus, claim 1 is directed to a process in which a compound (e.g., tibolone) is administered to a mammal "suffering from atherosclerosis." The preamble of claim 1 requires administration of the compound to inhibit the atherosclerotic process.

Claims 2-4 and 6 depend on claim 1. Claim 2 limits R_1 to H, OH, or O. Claim 3 limits R_3 to H, and requires the double bond to be in the 5, 10-position. Claims 2 and 3 read on a process of administering tibolone, since in tibolone R_1 = O and the double bond is in the 5,10 position. See Haenggi, Figure 1 (reproduced above). Claim 4 limits the administered compound to tibolone. Claim 6 requires the mammalian patient to be a human.

Claims 1-4 and 6 therefore read on administering tibolone to a human suffering from atherosclerosis, resulting in inhibition of the atherosclerotic process.

The Specification does not define the phrase "suffering from atherosclerosis." However, the Specification indicates that "atherosclerosis starts with the accumulation of cholesterol in lipoproteins in the vessel wall and the subsequent development of fatty streaks (probably the earliest macroscopically recognizable lesions). . . . Coronary heart disease (CHD) is a consequence of the atherosclerotic processes in the artery vessel wall." (Specification 1.)

"[I]n proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Sneed*, 710 F.2d 1544, 1548, 218 USPQ 385, 388 (Fed. Cir. 1983)

(citation omitted). Thus, we interpret the claims to encompass treating individuals having any degree of atherosclerosis, even if no adverse health effects (such as coronary heart disease) are outwardly visible.

2. APPEALED REJECTION

Claims 1-4 and 6 stand rejected under 35 U.S.C. § 103 as being obvious in view of Haenggi and Berglund.[2]

The Examiner cites Haenggi as teaching that administering tibolone to postmenopausal women decreases serum lipoprotein(a), a strong independent risk factor for coronary heart disease. (Answer 3.) The Examiner asserts that "Haenggi et al. does not teach expressly the employment of Tibolone in a method of inhibiting atherosclerosis." (*Id.* at 4.)

To meet this deficiency, the Examiner urges that "Berglund teaches that Lp(a) has been implicated with an increased risk of atherosclerosis, see the abstract." (*Id.*) The Examiner concludes that

> it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ Tibolone in a method of inhibiting atherosclerosis, e.g., by administering to a subject being suffering from atherosclerosis Tibolone.

(*Id.*)

Appellants argue that the rejection uses improper hindsight reasoning, and that the prior art does not teach or suggest administering tibolone to individuals suffering from atherosclerosis. (Br. 5; Reply Br. 1-2.)

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[2] Berglund, "Diet and drug therapy for lipoprotein (a)," *Current Opinion in Lipidology*, Vol. 6, pp. 48-56 (1995).

Specifically, Appellants urge that the Examiner fails to take into account Haenggi's disclosure that, despite tibolone's positive effect on lipoprotein(a), tibolone also significantly decreases serum HDL-cholesterol and apolipoprotein A-1. (Br. 6.)

Appellants argue that, when Haenggi is viewed in its entirety, it "does not teach or suggest the unexpectedly strong atheroprotective properties of tibolone." (*Id.*) As evidence of the unexpected properties of tibolone, Appellants urge that Table III of the Specification (page 17) demonstrates significantly better prevention of cholesterol accumulation and reduced fatty streak formation in the aortic arch, when compared with estradiol. (*Id.*)

The Examiner responds that the claims are not commensurate in scope with Appellants' alleged showing of unexpected results, because the data presented in the Specification were generated using rabbits, whereas the claims are directed to all mammals, including humans. (Answer 5-6.)

Our review of the references and arguments leads us to conclude that the Examiner did not rely on the most pertinent facts when considering Haenggi. In our view, Haenggi anticipates the appealed claims. We therefore vacate the Examiner's rejection and enter the following new ground of rejection.

3. NEW GROUND OF REJECTION

Under the provisions of 37 CFR § 41.50(b), we enter the following new ground of rejection: claims 1-4 and 6 are rejected under 35 U.S.C. § 102(b) as anticipated by Haenggi.

Haenggi describes the daily administration of 2.5 mg tibolone to post-menopausal women. (Haenggi 646, left col.) Daily administration of 2.5

mg tibolone is within Appellants' preferred dosage range. (Specification 6.) The amount of tibolone administered by Haenggi would therefore be effective to inhibit atherosclerosis, as required by the claims.

Haenggi does not expressly state that the tibolone recipients were "suffering from atherosclerosis," as required by the claims. However, as discussed *supra*, when properly interpreted in light of the specification, the language "suffering from atherosclerosis" reasonably encompasses individuals having any degree of atherosclerosis.

Moreover, Haenggi states that "the risk of coronary heart disease [is] known to be elevated in unsubstituted post menopausal women . . . ." (*Id.* at 649, right col.)[3] Also, the Specification states on page 1 that (emphasis added), "[c]oronary heart disease (CHD) is a consequence of atherosclerotic processes in the artery vessel wall. It is well known that the incidence of CHD in women in the reproductive stage of life is much lower than in men of similar age *but that the risks sharply increase following the menopause.*")

Because post-menopausal women are at elevated risk of atherosclerosis, Haenggi's treatment of post-menopausal women with tibolone would reasonably be expected to result in treatment of at least one patient "suffering from atherosclerosis," as required by claim 1. *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 77 USPQ2d 1321 (Fed. Cir. 2005), is

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[3] In this context, "unsubstituted" means not receiving hormone replacement therapy. *See* Haenggi, page 646, left-hand column ("[E]arly post menopausal women . . . [received] 6 months of hormone substitution with Tibolone 2.5 mg daily. The results were compared with a control group of 28 age-matched postmenopausal volunteers not wishing to receive hormonal substitution therapy.").

instructive. In *Perricone*, a claim was directed to a "method for preventing sunburn damage to exposed skin surfaces," by topically applying a defined composition. *Id.* at 1378, 77 USPQ2d at 1327. The claim was held to be anticipated by disclosure of a topical skin cream "because all skin surfaces are susceptible to sunburn damage." *Id.* at 1379, 77 USPQ2d at 1328.

That is, the claim was held to be anticipated because of the skin's susceptibility to sunburn, not because the prior art skin cream actually prevented sunburn every time it was applied. Similarly here, the claims are anticipated by Haenggi's administration of tibolone to a patient population known to be susceptible to atherosclerosis even if the method did not actually treat atherosclerosis in each of Haenggi's patients.

> [W]here the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.

In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).

Because the risk of coronary heart disease is elevated in post-menopausal women not receiving hormone replacement therapy, we find it reasonable to conclude that by administering tibolone to post-menopausal women, Haenggi administered tibolone to humans "suffering from atherosclerosis," given the breadth of that language. We therefore also conclude that, prima facie, Haenggi anticipates claims 1-4 and 6.

Appellants' arguments regarding motivation, hindsight, and unexpected results are not relevant to the issue of whether Haenggi anticipates claims 1-4 and 6. *In re Paulsen,* 30 F.3d 1475, 1482 n.11, 31

USPQ2d 1671, 1676 n.11 (Fed.Cir.1994) ("[E]vidence of nonobviousness is irrelevant for patentability purposes when an invention is anticipated under section 102.").

Thus, the fact that Appellants may have discovered that tibolone inhibits atherosclerosis does not establish patentability, because Haenggi previously described administering tibolone to a patient population known to include individuals suffering from atherosclerosis. As stated in *Perricone*, 432 F.3d at 1377-78, 77 USPQ2d at 1327 (citations omitted):

> [N]ew realization alone does not render the old invention patentable. Thus, when considering a prior art method, the anticipation doctrine examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure.

See also Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). ("[I]f granting patent protection on the disputed claim would allow the patentee to exclude the public from practicing the prior art, then that claim is anticipated, regardless of whether it also covers subject matter not in the prior art.").

To summarize, because Haenggi describes administering the claimed therapeutic agent to patients known to be at higher risk of atherosclerosis, it is reasonable to conclude that Haenggi anticipates claims 1-4 and 6. *In re Best, supra.* Because Appellants have not had the opportunity to address this rejection by argument or evidence, we designate it a new ground under 37 CFR § 41.50(b).

SUMMARY

We vacate the Examiner's obviousness rejection of claims 1-4 and 6, and enter a new ground of rejection of those claims based on anticipation.

TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review.

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner . . . .

(2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same record . . . .

VACATED, 37 CFR § 41.50(b)

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